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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,998	09/12/2003	David J. Ecker	DIBIS-0002US.P5	7721

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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 08/03/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/660,998	ECKER ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *13,15-20,22-25 and 29-45* is/are pending in the application.

4a) Of the above claim(s) *18 and 38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *13,15-17,19-20, 22-25,29-37 and 39-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 September 2003* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/03, 05/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restriction/election

1. Applicant's election without traverse of Group I (claims 1-25) in the reply filed on May 25, 2006 is acknowledged. Applicants' election of species (a human and complex I deficiency) is acknowledged.

Status

2. Claims 1-12, 14, 21, 26-28 are cancelled. New claims 29-45 are added. Claims 13, 16-19, 22 are amended. Claims 13, 15-17, 19-20, 22-25, 29-37, 39-45 read on elected Group I and species and considered for examination in this office action. Claims 18, 38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species.

Priority

3. This application filed on September 12, 2003 is a CIP of SU non-provisional 10/323,438 filed on 12/18/2002 ABN and is a CIP of 09/798,007 filed on 03/2/2001 ABN and claims benefit of 60/431,319 filed on 12/06/2002.

Information Disclosure Statement

4. The Information Disclosure Statement filed on December 29, 2003, and May 12, 2005 have been considered.

Informalities

5. The instant specification is reviewed for informalities:

(i) claims 16-19 depend on cancelled claims.

(ii) Fig. 20 A-B contains sequence which is not identified by SEQ ID No.

Correction is required.

Objection to the Specification

6. The specification is objected because of the following informalities:

(i) This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply the requirements of 37 CFR 1.821 through 1.825.

The instant application recites sequences that are not identified by SEQ ID No. (see at least Figure 20 A-20B) recite a nucleic acid sequence / amino acid sequence with more than 10 nucleotides or 4 amino acids, which is not identified by SEQ ID NO.).

(ii) The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code (see page 25, line 25). Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 16-17, 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 16-17 are dependent on cancelled claim 14 and claim 19 is dependent on cancelled claim 1. Thus the meets and bounds of the claims are unclear because it is not clear

what limitations the claims refer to. Amendment to recite proper dependency would obviate the rejection.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 22-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Gattermann et al. (Blood, Vol. 90, No. 12, pp. 4961-4972, 1997).

Gattermann et al. teach a method of characterizing heteroplasmy of a segment of mitochondrial DNA of an individual comprising (a) amplifying said segment of mitochondrial DNA (mtDNA) with a pair of primers to obtain a plurality of test amplification products corresponding to said segment (see page 4964, col. 2, paragraph 1);

(b) determining molecular masses of said plurality of amplification products (see page 4964, col. 2, paragraphs 2-4, indicating molecular masses are determined by gel electrophoresis);

(c) determining base compositions of said plurality of amplification products thereby characterizing said heteroplasmy (See page 4965, col. 1, paragraph 2 under results section, col. 2, paragraphs 1-3, page 4966, col. 1, paragraph 1).

With regard to claim 23, Gattermann et al. teach that the method further comprises obtaining a plurality of samples of mtDNA from said individual at different points of lifetime of the individual (see page 4964, col. 1, line 2-4, page 4965, col. 2, paragraph 1, page 4966, Fig. 3).

With regard to claim 24, Gattermann et al. teach that said method further comprises correlating the rate of naturally occurring mutations in mt DNA with the rate of onset of mitochondrial disease in plurality of individuals affected by mitochondrial disease (see page 4964, col. 2, paragraph 4, page 4966, col. 2, paragraph 1).

With regard to claim 25, Gattermann et al. teach that the method comprises complex I deficiency disease (see page 4962, Fig. 1, page 4963, Fig. 1, legend, col. 1, paragraph 1, under materials and methods section, col. 2, paragraphs 1-2).

B. Claims 22 is rejected under 35 U.S.C. 102(b) as being anticipated by Crespillo et al. (Int J Legal Med., Vol. 114, page 130-132, 2000) and A

Crespillo et al. teach a method of claim 22, of analyzing hypervariable regions of mitochondrial DNA comprising obtaining a database comprising plurality of known molecular masses (reference database) (see page 130, col. 2, paragraph 2 under materials and methods section characterizing heteroplasmy of a segment of mitochondrial DNA of an individual comprising (a) amplifying said segment of mitochondrial DNA (mtDNA) with a pair of primers to obtain a plurality of test amplification products corresponding to said segment (see page 130, col. 2, paragraph 1, under materials and methods);

(b) determining molecular masses of said plurality of amplification products (see page 130, col. 2, paragraph 2 under materials and methods section, indicating molecular masses are determined by sequencer);

(c) determining base compositions of said plurality of amplification products thereby and comparing with the molecular masses of reference database thereby characterizing heteroplasmy

(see page 130, abstract, col. 2, paragraph 2 under materials and methods section). Accordingly Crespillo et al. anticipates the instant claims.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 13, 15-17, 19-20, 29-37, 39-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gattermann et al. (Blood, Vol. 90, No. 12, pp. 4961-4972, 1997) in view of Crespillo et al. (Int J Legal Med., Vol. 114, page 130-132, 2000) and Aserud et al. (Am Soc Mass spectrometry, Vol. 7, page 1266-1269, 1996).

Gattermann et al. teach a method for characterizing heteroplasmy in mtDNA as discussed in section 8A above.

With regard to claims 13, 15, 34. 35, Gattermann et al. also teach digesting amplified PCR products with restriction enzymes that include Rsa I prior to determining the heteroplasmy (see page 4964, col. 2, paragraph 2).

With regard to claims 16-17, 36-37, Gattermann et al teach that said subjects are humans (see page 4964, col. 1, line 2-10).

However Gatterman et al. did not teach obtaining a database comprising known molecular masses of mtDNA fragments and determining base composition by mass spectrometry.

Crespillo et al. teach a method of analyzing hypervariable regions of mitochondrial DNA comprising obtaining a database comprising plurality of known molecular masses (reference database) (see page 130, col. 2, paragraph 2 under materials and methods section characterizing heteroplasmy of a segment of mitochondrial DNA of an individual comprising (a) amplifying said segment of mitochondrial DNA (mtDNA) with a pair of primers to obtain a plurality of test amplification products corresponding to said segment (see page 130, col. 2, paragraph 1, under materials and methods);

(b) determining molecular masses of said plurality of amplification products (see page 130, col. 2, paragraph 2 under materials and methods section, indicating molecular masses are determined by sequencer);

(c) determining base compositions of said plurality of amplification products thereby and comparing with the molecular masses of reference database (see page 130, col. 2, paragraph 2 under materials and methods section).

Aaserud et al. teach a method for accurate measurement of base composition of double-stranded DNA by mass spectrometry (see page 1266, abstract, page 1268, col. 1, paragraph 3), wherein Aaserud et al. teach that the method provides accurate molecular weights of its high-resolution mass spectrum from an electrospray ionization/Fourier transform instruments yielding only the correct ds- and ss- base compositions (see page 1266, abstract).

It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to modify the method of mtDNA analysis as taught by Gattermann et al. in a manner as taught by Crespillo et al. by incorporating a mtDNA database comprising known molecular masses and as taught by Aaserud et al. by incorporating measuring base-composition by mass spectrometry for the purpose of enhancing sensitivity of the method for analyzing sequence variations in said target nucleic acid. One skilled in the art would have been motivated to combine the method of analyzing mtDNA as taught by Gattermann et al. with a step of including mtDNA database with known masses as taught by Crespillo et al. and base-composition measurement by using mass spectrometry as taught by Aaserud et al. because the ordinary artisan would have a reasonable expectation of success that inclusion of said limitations would result in a sensitive comparison of sequence variations in mtDNA and accurate measurement of base compositions in said target because Crespillo et al. explicitly taught that the use of a mtDNA database would result in estimating the frequency of different sequence variations of mtDNA (see abstract on page 130) and Aaserud et al. explicitly taught that the mass spectrometry measures accurate molecular masses thereby providing correct base compositions of a target nucleic acid (see abstract on page 1266) and such modification is considered as obvious over cited prior art in the absence of secondary considerations.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 571-272-0783. The examiner can normally be reached on 8.30A.M. - 4.30P.M , Mon - Friday,.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Suryaprabha Chunduru
Primary Examiner
Art Unit 1637

Prabha Chunduru 7/31/06
SURYAPRABHA CHUNDURU
PATENT EXAMINER